APPLICANTS' REQUEST FOR AN INTERFERENCE WITH A PATENT

1. Identification of Patent under Rule 607(a)(1)

Applicants seek an interference between this application and United States Patent No. 5,567,413 to Klaveness et al* (hereinafter the '413 patent) which issued on October 22, 1996.

2. Presentation of a proposed Count Under Rule 607(a)(2)

For purposes of this rule, the following proposed count is believed to define overlapping, patentably indistinct subject matter between this application and the '413 patent:

Count 1

Microbubbles comprising an amphiphilic phospholipid material capable of formation of gas-containing microbubbles, said microbubbles comprising a physiologically acceptable halogenated gas or

a process of preparing a contrast agent comprising generating said bubbles.

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* The '413 patent is a division of U.S. 5,536,490 from which Applicants copied claims into the subject application in a preliminary amendment filed with the original application papers on July 15, 1997.

3. Identification of Claims from the '413 Patent that Correspond to the Proposed Count under Rule 607(a)(3)

Proposed Count	'413 Patent Claims that Correspond to Proposed Count
Count 1	3-10, 19, 20, 23, 24, 33-37, 44 and 46

4. Compliance with Rule 607(a)(4)

a. Presentation of New Claims Corresponding to the Proposed Count under Rule 607(a)(4)

Applicants have added new claims 77-79 which are believed to correspond to Count 1, i.e., define patentably indistinct subject matter.

b. Explanation of Why Each Claim Corresponds to the Proposed Count

i) Applicants' Claims Corresponding to Count 1

Claim 77 corresponds exactly to proposed Count 1.

Claims 78 and 79 substantially correspond to Count 1. These claims differ from Count 1 by reciting "fluorine-containing gas" and "freon", respectively, instead of the "physiologically acceptable halogenated gas" of Count 1. However, claims 78 and 79 define subsets of Count 1 because both "fluorine-containing gas" and "freon" are subsets of Count 1's "physiologically acceptable halogenated gas."

This is demonstrated by Applicants' specification at page 15, lines 22-25 which states that:

> "The gases in the microbubbles of the present invention can include, in addition to current innocuous physiologically acceptable gases like CO_2, nitrogen, N_2O, methane, butane, freon and mixtures thereof..." (emphasis added).

The gases defined by "fluorine-containing gases" include "freon". *Hawley's Condensed Chemical Dictionary*, Twelfth Edition, Revised by Richard J. Lewis, Sr., Van Nostrand Reinhold Co., New York.

The '413 patent at column 2, lines 29-34 includes a similar definition:

> Any biocompatible gas may be employed in the contrast agents of the invention, for example air, nitrogen, oxygen, hydrogen, nitrous oxide, carbon dioxide, helium, argon, sulphur hexafluoride and low molecular weight optionally fluorinated hydrocarbons such as methane, acetylene or carbon tetrafluoride...(emphasis added).

ii. The '413 Claims Corresponding to Count 1

Claim 3 of the '413 patent is the same as Count 1 except for its recitation of fluorinated low molecular weight hydrocarbon as its physiologically acceptable gas. Applicants submit that for the reasons stated in Section 4, b, i, *supra*, this is an immaterial limitation for purposes of this analysis, i.e., it can be disregarded in

evaluating the separate or common patentability of the '413 patent claims and e.g., claims 77-79 of this application. The other claims that correspond to Count 1 of the '413 patent (3-10, 19, 20, 23, 33-37, 44 and 46) relate to specific, patentably indistinct aspects of the microbubbles which are all encompassed by Count 1.

5. Application of the Terms of Applicants' Claims 75-77 Which Correspond to Proposed Count 1 to Applicants' Specification Under Rule 607(a)(5)

Claims	Citations to Applicants' Specification (and Parent Application EP 90810262.7 in parentheses)[1]
Microbubbles comprising	the suspension of microbubbles according to the invention at p. 6, l. 27-28 (p. 5, l. 26-27)
an amphiphilic phospholipid material	amphipatic compounds...particularly phospholipids at p. 6, l. 4 and 7 (p. 5, l. 15-20)
capable of formation of gas-containing microbubbles	then air or a gas is introduced into the liposome solution so that a suspension of microbubbles will form at p. 6, l. 36-p. 7, 1. 1 (p. 5, l. 35-36)
said microbubbles comprising a physiologically acceptable halogenated gas (Claim 77); fluorine-containing gas (Claim 78); freon (Claim 79)	the gases in the microbubbles of the present invention can include in addition to current innocuous physiologically acceptable gases like...freon at p. 15, l. 22-24 (p. 14, l. 11-13)

The citations to EP 90810262.7, Applicants' parent application, demonstrate that Applicants are entitled to the benefit of this EP application for claims 75-77.

6. Explanation of Compliance with 35 U.S.C. § 135(b) Under Rule 607(a)(6)

This request for an interference complies with 35 U.S.C.§ 135(b) because it has been filed before October 22, 1997 which is within one year of the October 22, 1996 issue date of the '413 patent, and it adds claims that are the same or substantially the same as claims in the '413 patent.

7. Other Interfering, Patentably Indistinct Subject Matter

The '413 patent has claims directed to other subject matter which is disclosed and claimed in Applicants' application. The table below summarizes the patentably indistinct subject matter:

'413 Claimed Subject matter	'413 Claims	Applicants' Claims	Support for Applicants' Claims in Applicants' Specification (and Parent Application EP90810262.7 in parentheses)
Aqueous dispersion	7-10	62-65	See chart on page 9 herein and aqueous dispersion at pp. 1, 5-6, 13-14, specific phospholipid and additives at pp. 9-11, and microbubble concentration at pp. 12-14 of the disclosure (pp. 1, 4-6, 9-13)
Process for preparing a contrast agent	33-37	70-74	See chart on page 9 herein and process variables at pp. 1, 5-13 of the disclosure (pp. 1, 4-14)

[1] Copy of Schneider et al.'s foreign application EP 90810262.7 is attached hereto.

Contrast Agent prepared by a process	44	75	See chart on page 9 herein and contrast agent at pp. 1, 14-15 and the examples of the disclosure pp. 1, 13-14 (p. 1 and examples)
Method of enhancing images of vascular system	46	76	See chart on page 9 herein and method of enhancing at pp. 1, 14-15 and the examples of the disclosure (p. 1 and examples)

The citations to EP 90810262.7, Applicants' parent application, demonstrate that Applicants are entitled to the benefit of this EP application for claims 57-77.

The count directed to this subject matter should be '413 claims 3 and 22 combined, (1) written in independent claim form, and (2) with "physiologically acceptable halogenated gas" substituted for "fluorinated low molecular weight hydrocarbon." The count would encompass all of the subject matter of the '413 claims and Applicants' claims which are identified above -- the differences between the claims and the count are all recitations of more specific, patentably indistinct, elements of the count. For example, the fluorinated low molecular weight hydrocarbon of the '413 claims is patentably indistinct from the physiologically acceptable gas of the count (see discussion *supra* regarding

proposed Count 1). Section 135(b) is complied with for this new count and claims for the reasons stated in Section 6, *supra.*

Please examine this application and act on this amendment with special dispatch as provided by 37 C.F.R. 1.607(b).

Respectfully submitted,

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